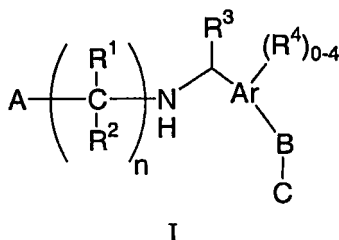


WHAT IS CLAIMED IS:

1. A compound of Formula I



5

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

- 10 Ar is phenyl or naphthyl;

A is selected from: $-\text{CO}_2\text{H}$, 1*H*-tetrazol-5-yl, $-\text{PO}_3\text{H}_2$, $-\text{PO}_2\text{H}_2$, $-\text{SO}_3\text{H}$, and $-\text{PO}(\text{R}^5)\text{OH}$, wherein R^5 is selected from the group consisting of: C_{1-4} alkyl, hydroxy C_{1-4} alkyl, phenyl, $-\text{C}(\text{O})-\text{C}_{1-3}$ alkoxy and $-\text{CH}(\text{OH})$ -phenyl, said phenyl and phenyl portion of $-\text{CH}(\text{OH})$ -phenyl optionally substituted with 1-3 substituents independently selected from the group consisting of: hydroxy, halo, $-\text{CO}_2\text{H}$, C_{1-4} alkyl, $-\text{S}(\text{O})_k\text{C}_{1-3}$ alkyl, wherein k is 0, 1 or 2, C_{1-3} alkoxy, C_{3-6} cycloalkoxy, aryl and aralkoxy, the alkyl portions of said C_{1-4} alkyl, $-\text{S}(\text{O})_k\text{C}_{1-3}$ alkyl, C_{1-3} alkoxy and C_{3-6} cycloalkoxy optionally substituted with 1-3 halo groups;

15

n is 2, 3 or 4;

20

each R^1 and R^2 is each independently selected from the group consisting of: hydrogen, halo, hydroxy, $-\text{CO}_2\text{H}$, C_{1-6} alkyl and phenyl, said C_{1-6} alkyl and phenyl optionally substituted with 1-3 halo groups;

25

R^3 is selected from the group consisting of: hydrogen and C_{1-4} alkyl, optionally substituted with 1-3 hydroxy or halo groups;

- 30 each R^4 is independently selected from the group consisting of: hydroxy, halo,

-CO₂H, C₁₋₄alkyl, -S(O)_kC₁₋₃alkyl, wherein k is 0, 1 or 2, C₁₋₃alkoxy, C₃₋₆cycloalkoxy, aryl and aralkoxy, the alkyl portions of said C₁₋₄alkyl, -S(O)_kC₁₋₃alkyl, C₁₋₃alkoxy and C₃₋₆cycloalkoxy optionally substituted with 1-3 halo groups;

5 C is selected from the group consisting of:

- (1) C₁₋₈alkyl, C₁₋₈alkoxy, -(C=O)-C₁₋₆alkyl or -CHOH-C₁₋₆alkyl, said C₁₋₈alkyl, C₁₋₈alkoxy, -(C=O)-C₁₋₆alkyl and -CHOH-C₁₋₆alkyl optionally substituted with phenyl, and
 - (2) phenyl or HET, each optionally substituted with 1-3
- 10 substituents independently selected from the group consisting of: halo, phenyl, C₁₋₄alkyl and C₁₋₄alkoxy, said C₁₋₄alkyl and C₁₋₄alkoxy groups optionally substituted from one up to the
- 15 maximum number of substitutable positions with a substituent independently selected from halo and hydroxy, and said phenyl optionally substituted with 1 to 5 groups independently selected from the group consisting of : halo and C₁₋₄alkyl, optionally substituted with 1-3 halo groups,

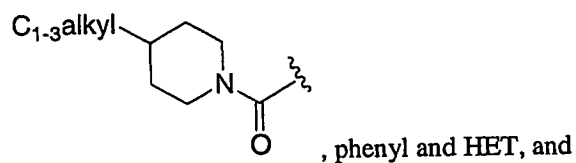
or C is not present;

20

when C is not present then B is selected from the group consisting of: phenyl, C₅₋₁₆alkyl, C₅₋₁₆alkenyl, C₅₋₁₆alkynyl, -CHOH-C₄₋₁₅alkyl, -CHOH-C₄₋₁₅alkenyl, -CHOH-C₄₋₁₅alkynyl, C₄₋₁₅alkoxy, -O-C₄₋₁₅alkenyl, -O-C₄₋₁₅alkynyl, C₄₋₁₅alkylthio, -S-C₄₋₁₅alkenyl, -S-C₄₋₁₅alkynyl, -CH₂-C₃₋₁₄alkoxy, -CH₂-O-C₃₋₁₄alkenyl, -CH₂-O-C₃₋₁₄alkynyl, -(C=O)-C₄₋₁₅alkyl, -(C=O)-C₄₋₁₅alkenyl, -(C=O)-C₄₋₁₅alkynyl, -(C=O)-O-C₃₋₁₄alkyl, -(C=O)-O-C₃₋₁₄alkenyl, -(C=O)-O-C₃₋₁₄alkynyl, -(C=O)-N(R⁶)(R⁷)-C₃₋₁₄alkyl, -(C=O)-N(R⁶)(R⁷)-C₃₋₁₄alkenyl, -(C=O)-N(R⁶)(R⁷)-C₃₋₁₄alkynyl, -N(R⁶)(R⁷)-(C=O)-C₃₋₁₄alkyl, -N(R⁶)(R⁷)-(C=O)-C₃₋₁₄alkenyl and -N(R⁶)(R⁷)-(C=O)-C₃₋₁₄alkynyl,

30

when C is phenyl or HET then B is selected from the group consisting of: C₁₋₆alkyl, C₁₋₅alkoxy, -(C=O)-C₁₋₅alkyl, -(C=O)-O-C₁₋₄alkyl, -(C=O)-N(R⁶)(R⁷)-C₁₋₄alkyl,

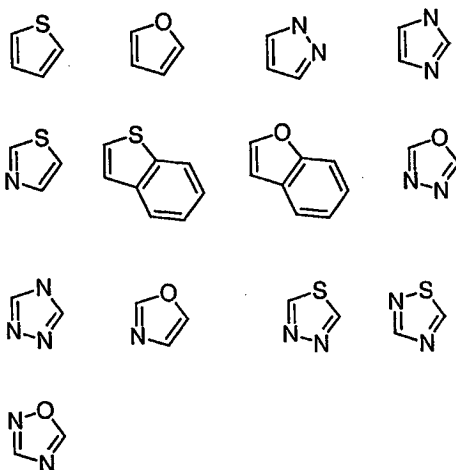


when C is C₁₋₈alkyl, C₁₋₈alkoxy, -(C=O)-C₁₋₆alkyl or -CHOH-C₁₋₆alkyl then B is
 5 phenyl; and

R⁶ and R⁷ are independently selected from the group consisting of: hydrogen, C₁₋₉alkyl and -(CH₂)_p-phenyl, wherein p is 1 to 5 and phenyl is optionally substituted
 with 1-3 substituents independently selected from the group consisting of: C₁₋₃alkyl
 10 and C₁₋₃alkoxy, each optionally substituted with 1-3 halo groups.

2. The compound according to Claim 1 wherein HET is selected
 from the group consisting of:

15



3. The compound according to Claim 1 wherein n is 2.
4. The compound according to Claim 1 wherein n is 3.

5. The compound according to Claim 3 wherein each R¹ and R² is independently selected from the group consisting of: hydrogen, -CO₂H, hydroxy, halo, C₁₋₃alkyl and phenyl.
- 5 6. The compound according to Claim 1 wherein A is PO₃H₂.
7. The compound according to Claim 1 wherein A is -CO₂H.
8. The compound according to Claim 1 wherein A is PO(R⁵)OH,
10 wherein R⁵ is selected from the group consisting of: C₁₋₄alkyl, hydroxyC₁₋₄alkyl, C(O)-C₁₋₂alkoxy and benzyl, wherein both the methyl and phenyl portions of said benzyl are optionally substituted with 1-3 halo or hydroxy groups.
9. The compound according to Claim 1 wherein A is PO₂H₂.
- 15 10. The compound according to Claim 1 wherein A is 1*H*-tetrazol-5-yl.
11. The compound according to Claim 1 wherein R³ is hydrogen or
20 methyl.
12. The compound according to Claim 1 wherein each R⁴ is independently selected from the group consisting of: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkylthio, phenyl, benzyloxy and cyclopropyloxy.
- 25 13. The compound according to Claim 1 wherein B is C₈₋₁₀alkyl and C is not present.
14. The compound according to Claim 1 wherein B is C₄₋₁₁alkoxy
30 and C is not present.
15. The compound of according to Claim 1 wherein B is phenyl, optionally substituted with 1-3 substituents independently selected from the group

consisting of: halo, C₁₋₄alkyl and C₁₋₄alkoxy, and C is selected from the group consisting of: hydrogen, phenyl, C₁₋₈alkyl, C₁₋₈alkoxy, -(C=O)-C₁₋₆alkyl and -CHOH-C₁₋₆alkyl, said C₁₋₈alkyl, C₁₋₈alkoxy, -(C=O)-C₁₋₆alkyl and -CHOH-C₁₋₆alkyl optionally substituted with phenyl.

5

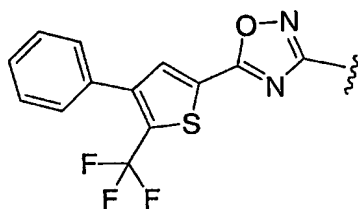
16. The compound according to Claim 1 wherein B is selected from the group consisting of: -CHOH-C₆₋₁₀alkyl, C₆₋₁₀alkylthio, -CH₂-C₅₋₉alkoxy, -(C=O)-C₆₋₁₀alkyl, -(C=O)-O-C₅₋₉alkyl, -(C=O)-N(R⁶)(R⁷)-C₅₋₉alkyl, -N(R⁶)(R⁷)-(C=O)-C₅₋₉alkyl, and C is not present.

10

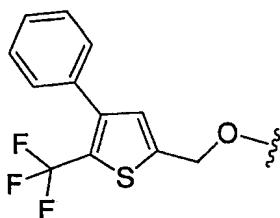
17. The compound according to Claim 1 wherein B is C₁₋₆alkyl or C₁₋₅alkoxy and C is phenyl.

18. The compound according to Claim 1 wherein B-C is

15



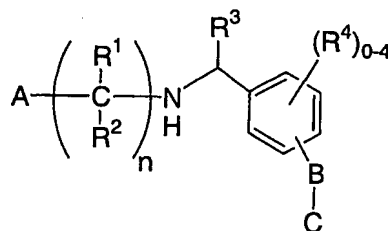
or



19. The compound according to Claim 1 wherein Ar is phenyl and the group -B-C is attached to the phenyl ring at the 3- or 4-position.

20

20. A compound of Formula II



II

or a pharmaceutically acceptable salt or hydrate thereof, wherein

5

the group -B-C is attached to the phenyl ring at the 3- or 4-position;

n is 2, 3 or 4;

each R¹ and R² is independently selected from the group consisting of: hydrogen, -
10 CO₂H, hydroxy, halo, C₁-3alkyl and phenyl, said C₁-3alkyl and phenyl optionally
substituted with 1-3 halo group;

A is selected from the group consisting of: 1H-tetrazol-5-yl, PO₂H₂, PO₃H₂, -CO₂H
and PO(R⁵)OH, wherein R⁵ is selected from the group consisting of: C₁-4alkyl,
15 hydroxyC₁-4alkyl, C(O)-C₁-2alkoxy and benzyl, wherein both the methyl and phenyl
portions of said benzyl are optionally substituted with 1-3 halo or hydroxy groups;

R³ is hydrogen or methyl;

each R⁴ is independently selected from the group consisting of: halo, hydroxy, C₁-
20 3alkyl, C₁-3alkoxy, C₁-3alkylthio, phenyl, benzyloxy and cyclopropyloxy; and

B-C is selected from the group consisting of:

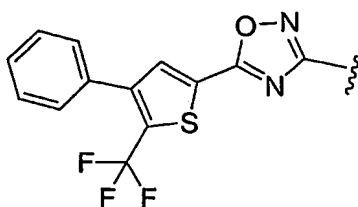
- (1) B is C₈-10alkyl and C is not present.
25 (2) B is C₄-11alkoxy and C is not present.
(3) B is phenyl, optionally substituted with 1-3 substituents
independently selected from the group consisting of: halo, C₁-4alkyl and C₁-4alkoxy,
and C is selected from the group consisting of: hydrogen, phenyl, C₁-8alkyl, C₁-
galkoxy, -(C=O)-C₁-6alkyl and -CHOH-C₁-6alkyl, said C₁-8alkyl, C₁-8alkoxy, -
30 (C=O)-C₁-6alkyl and -CHOH-C₁-6alkyl optionally substituted with phenyl;

(4) **B** is -CHOH-C₆₋₁₀alkyl, C₆₋₁₀alkylthio, -CH₂-C₅₋₉alkoxy, -
(C=O)-C₆₋₁₀alkyl, -(C=O)-O-C₅₋₉alkyl, -(C=O)-N(R⁶)(R⁷)-C₅₋₉alkyl or -
N(R⁶)(R⁷)-(C=O)-C₅₋₉alkyl, and **C** is not present.

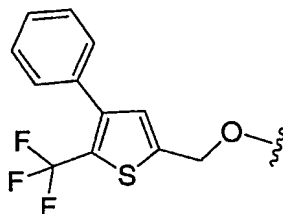
(5) **B** is C₁₋₆alkyl or C₁₋₅alkoxy and **C** is phenyl.

(6) **B-C** is

5

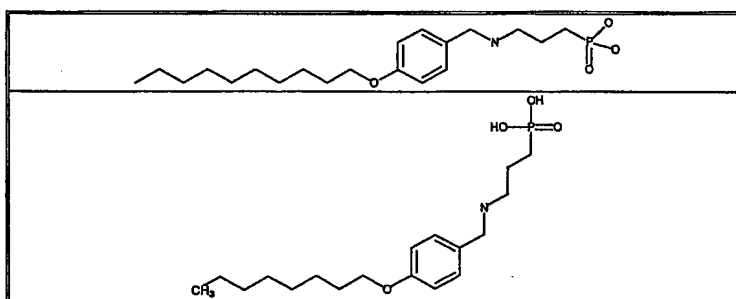


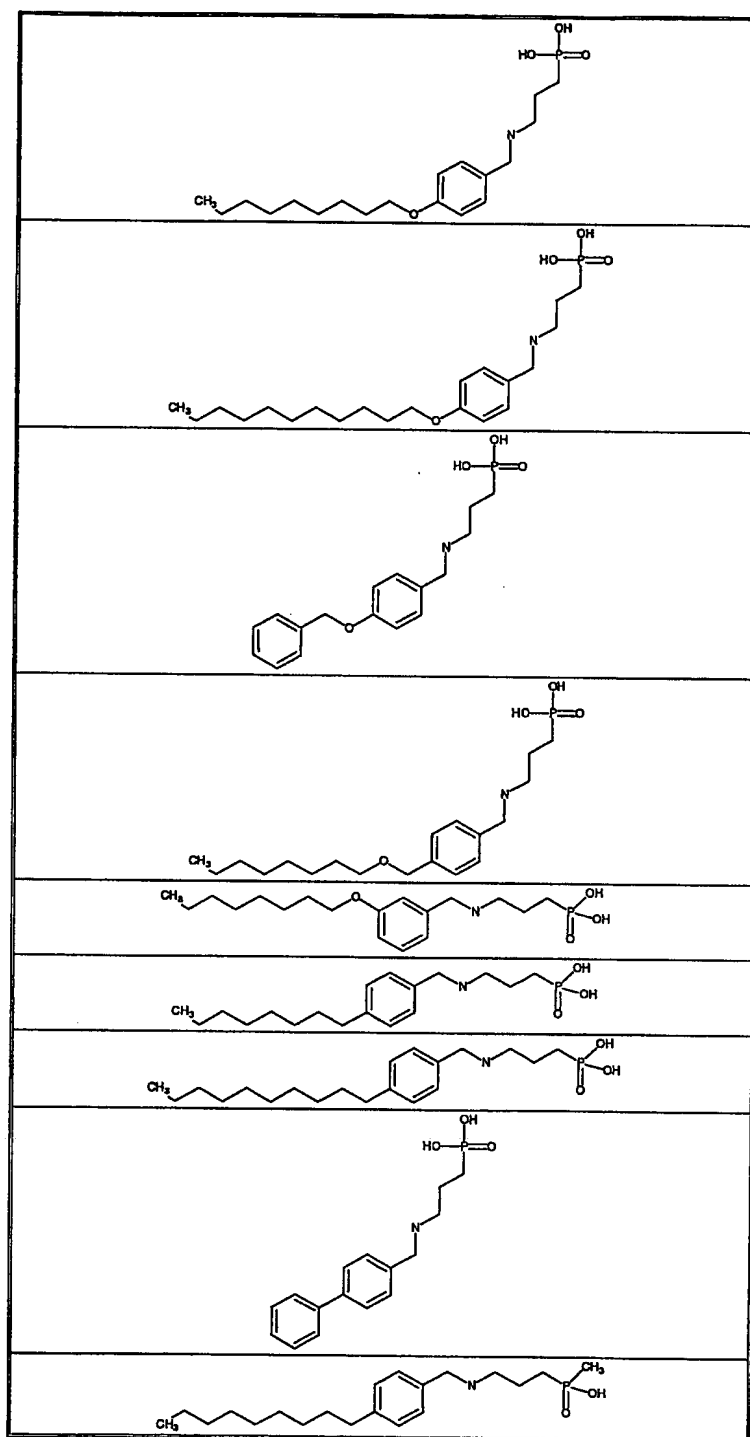
or

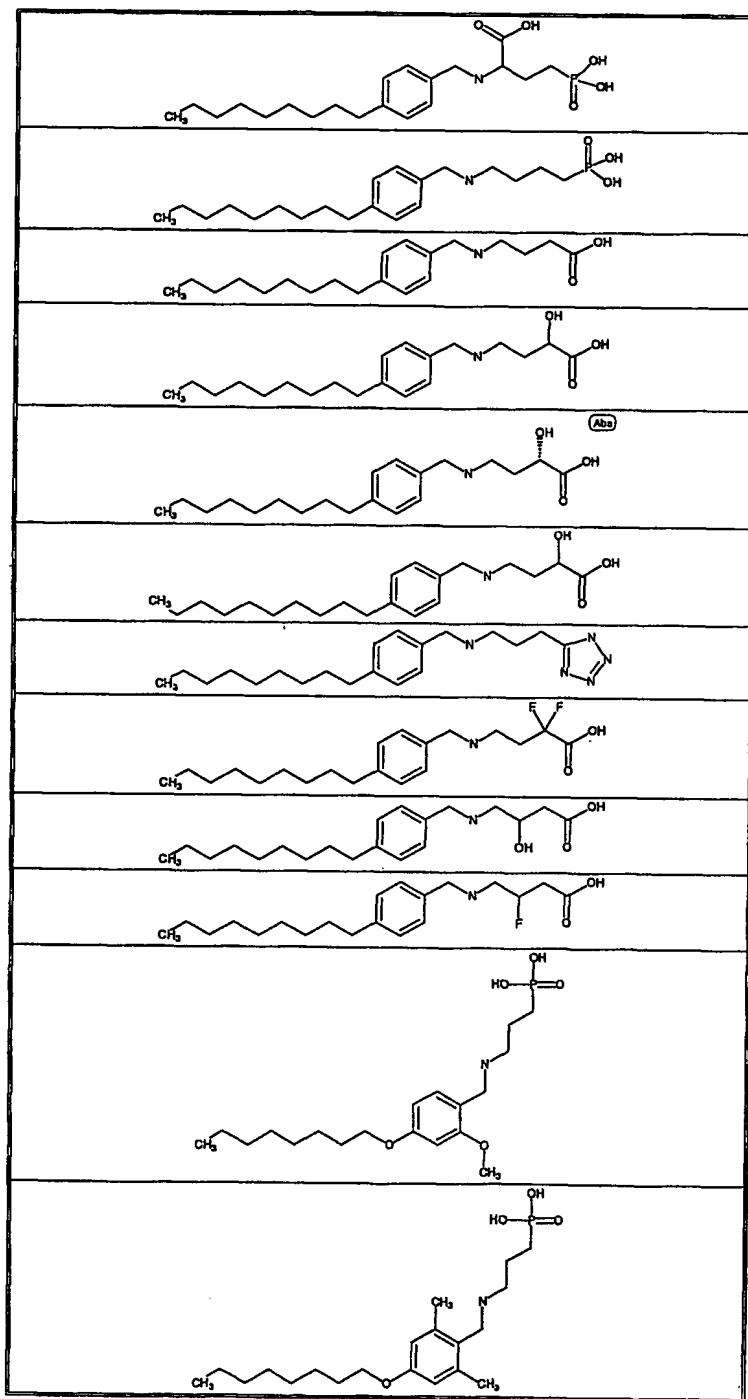


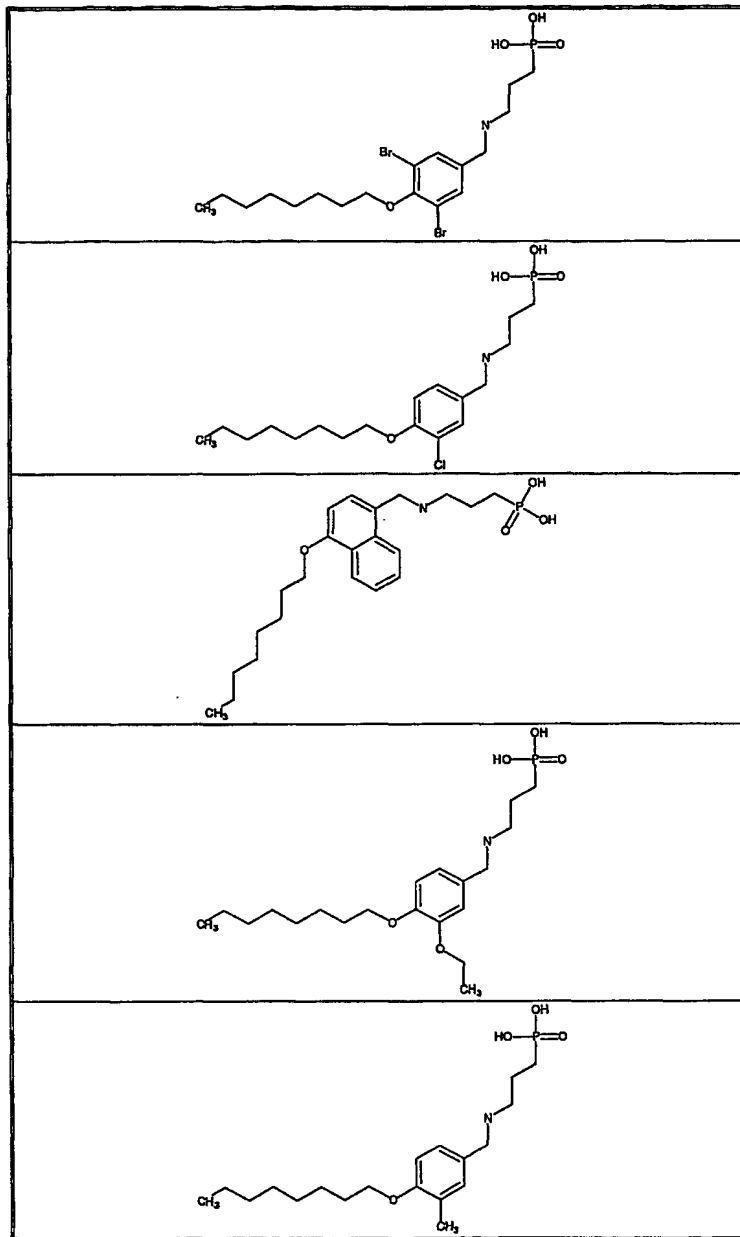
21. A compound selected from the group consisting of:

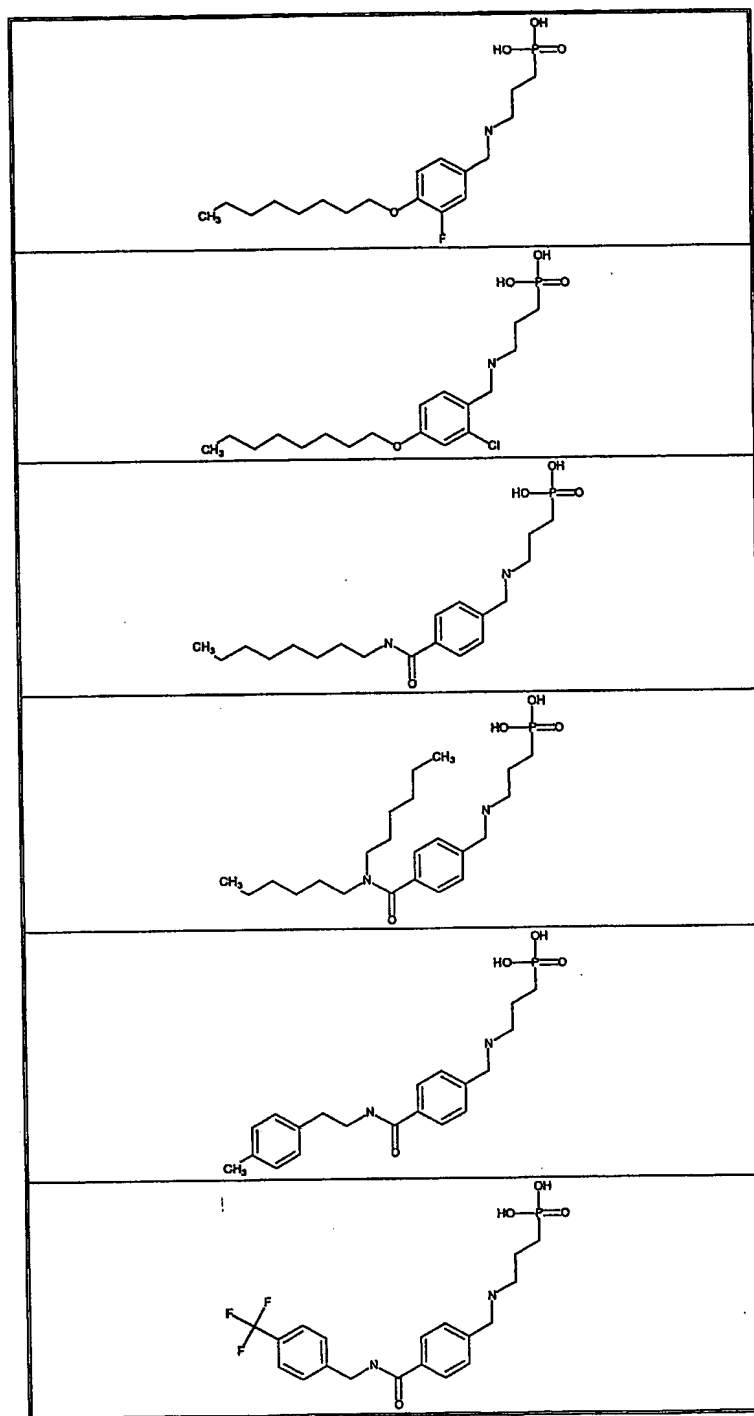
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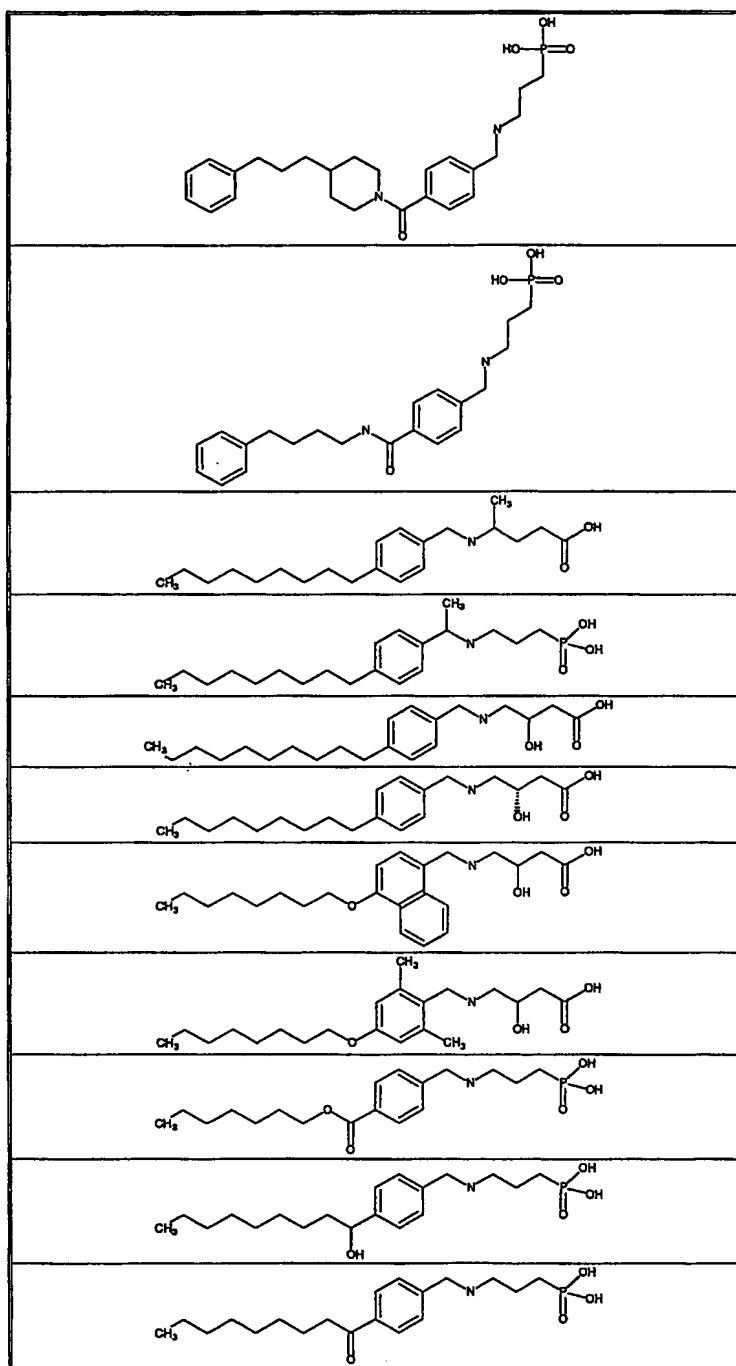


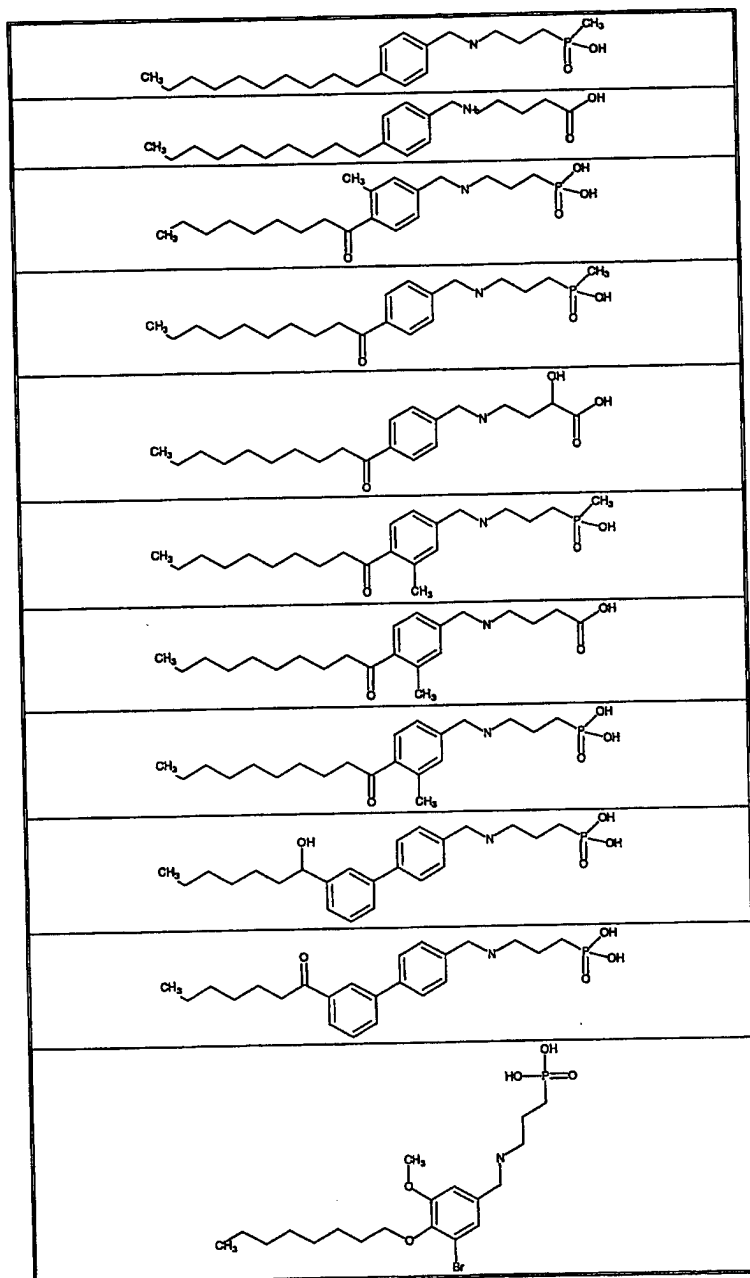


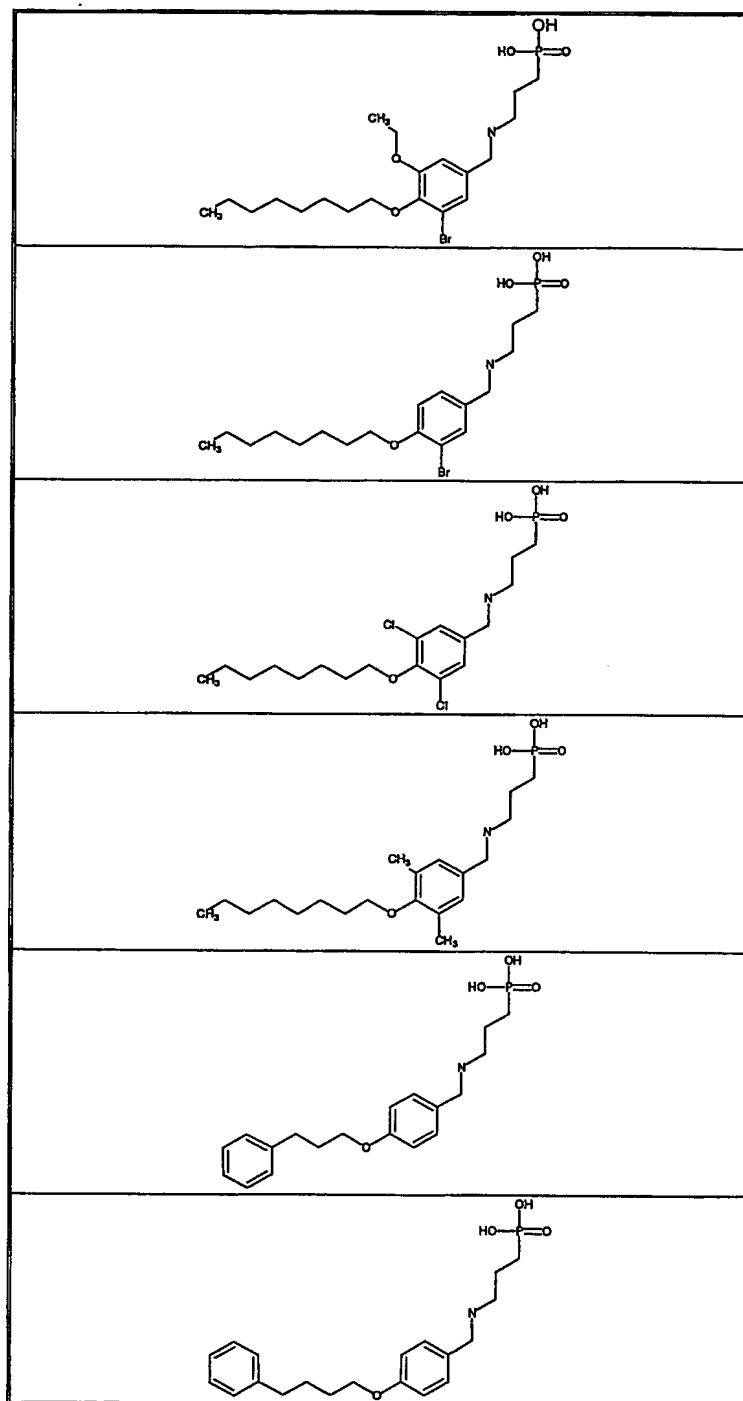


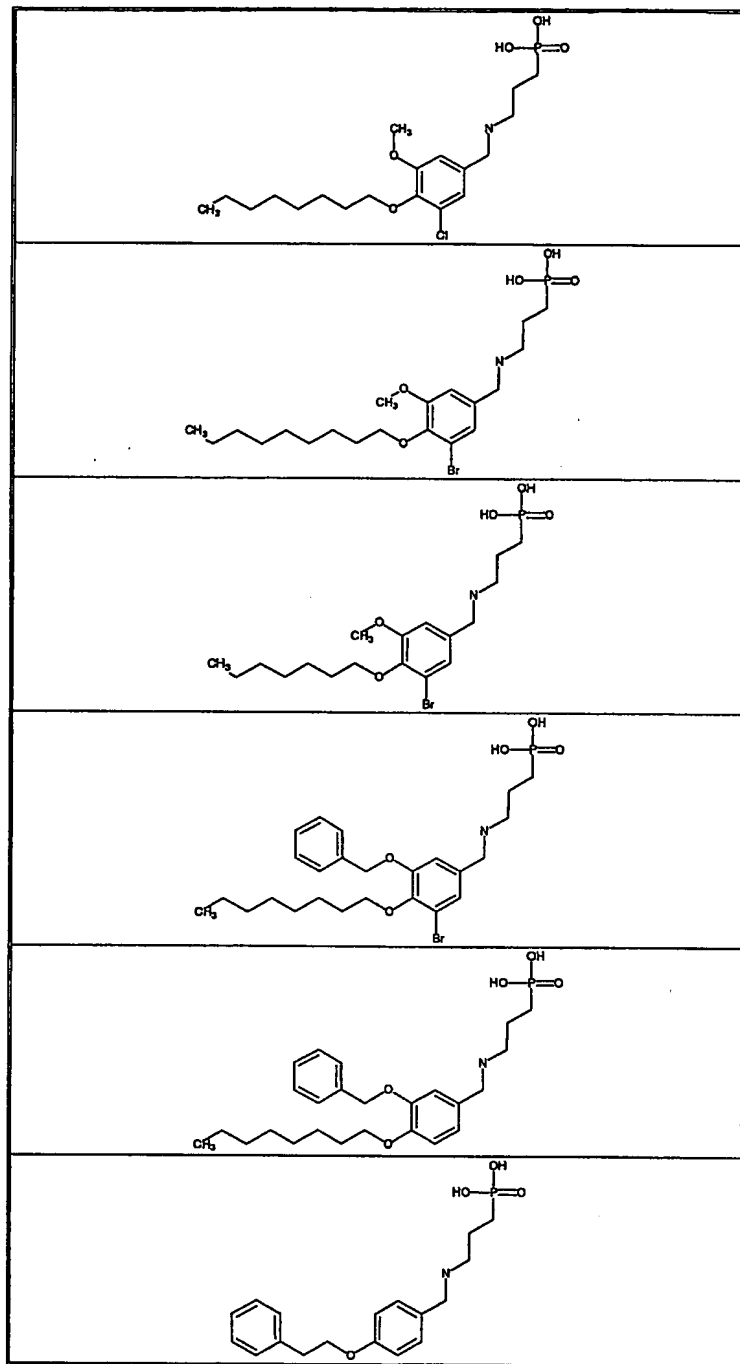


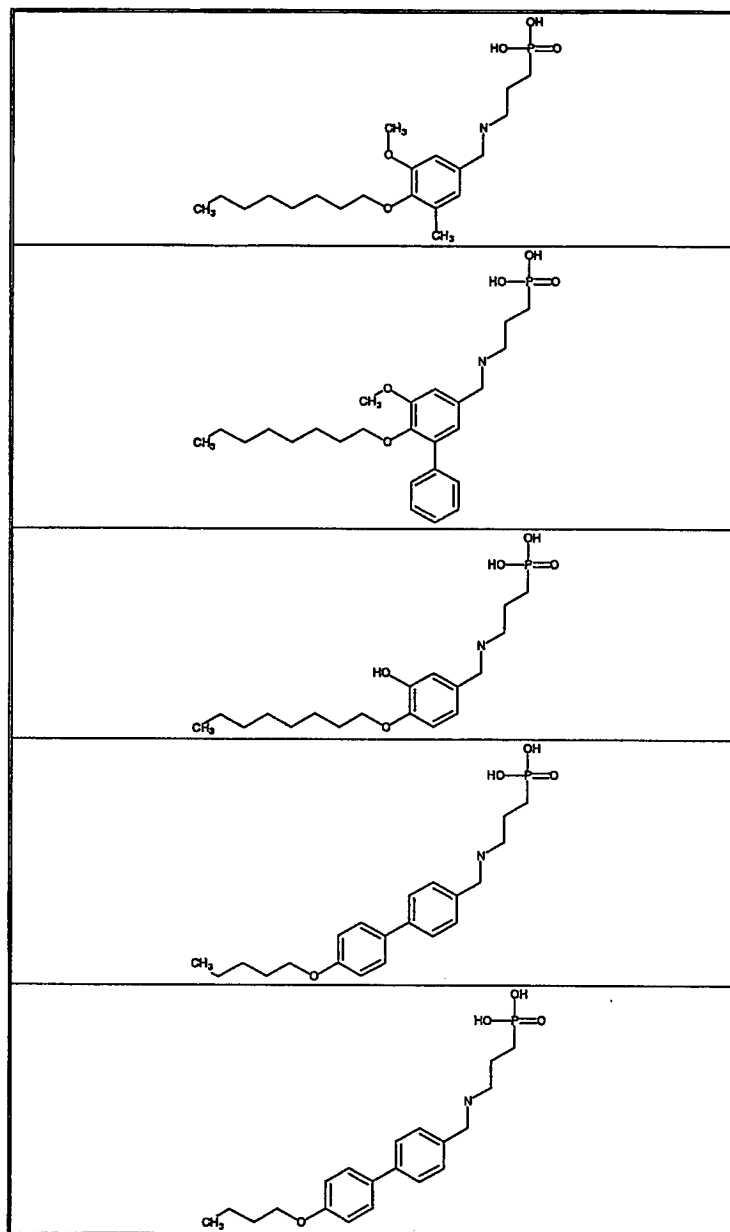


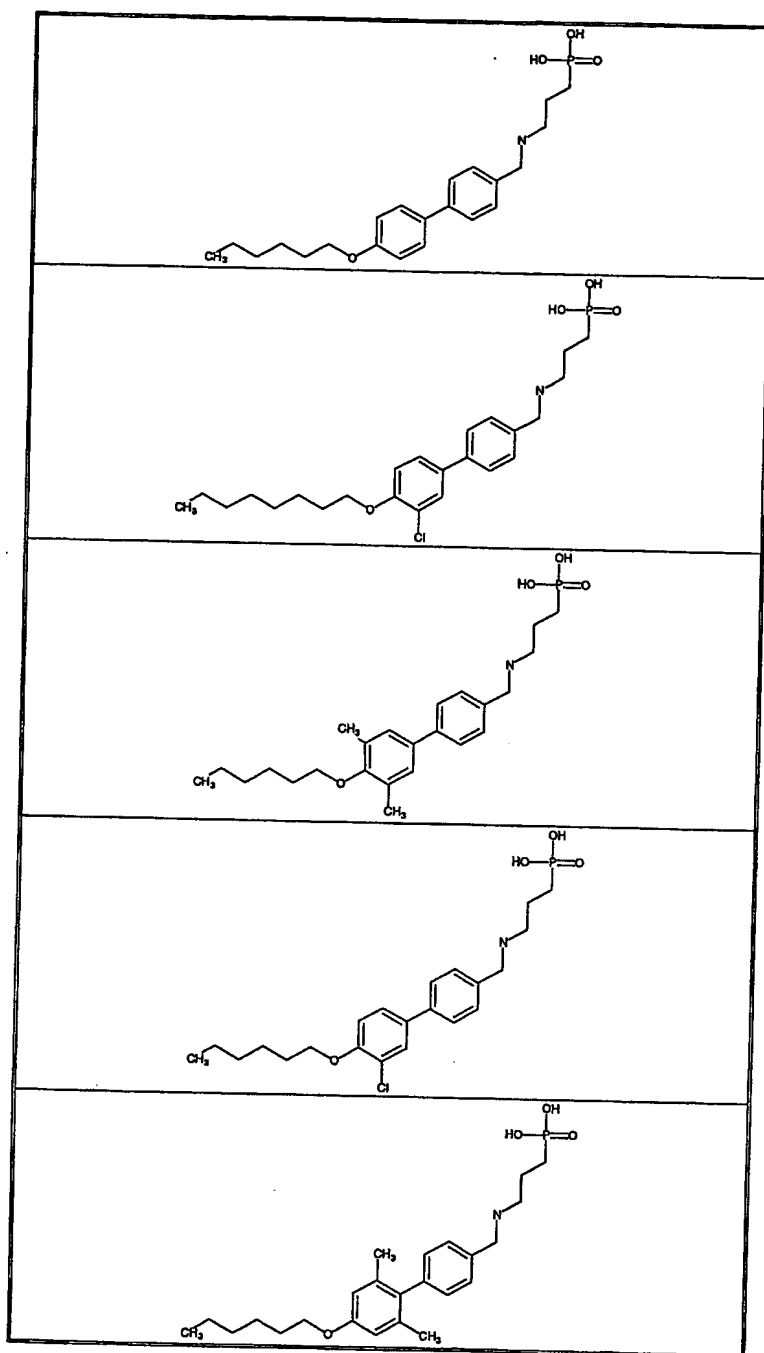


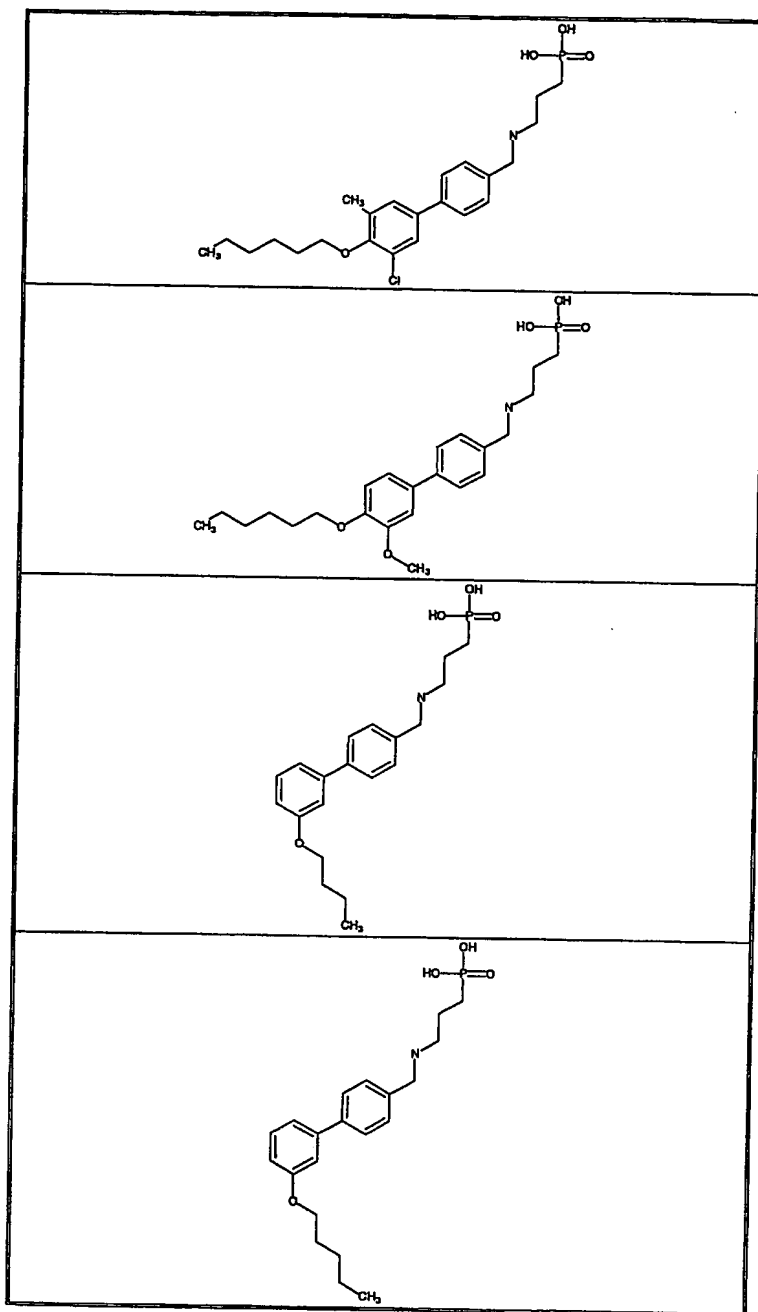


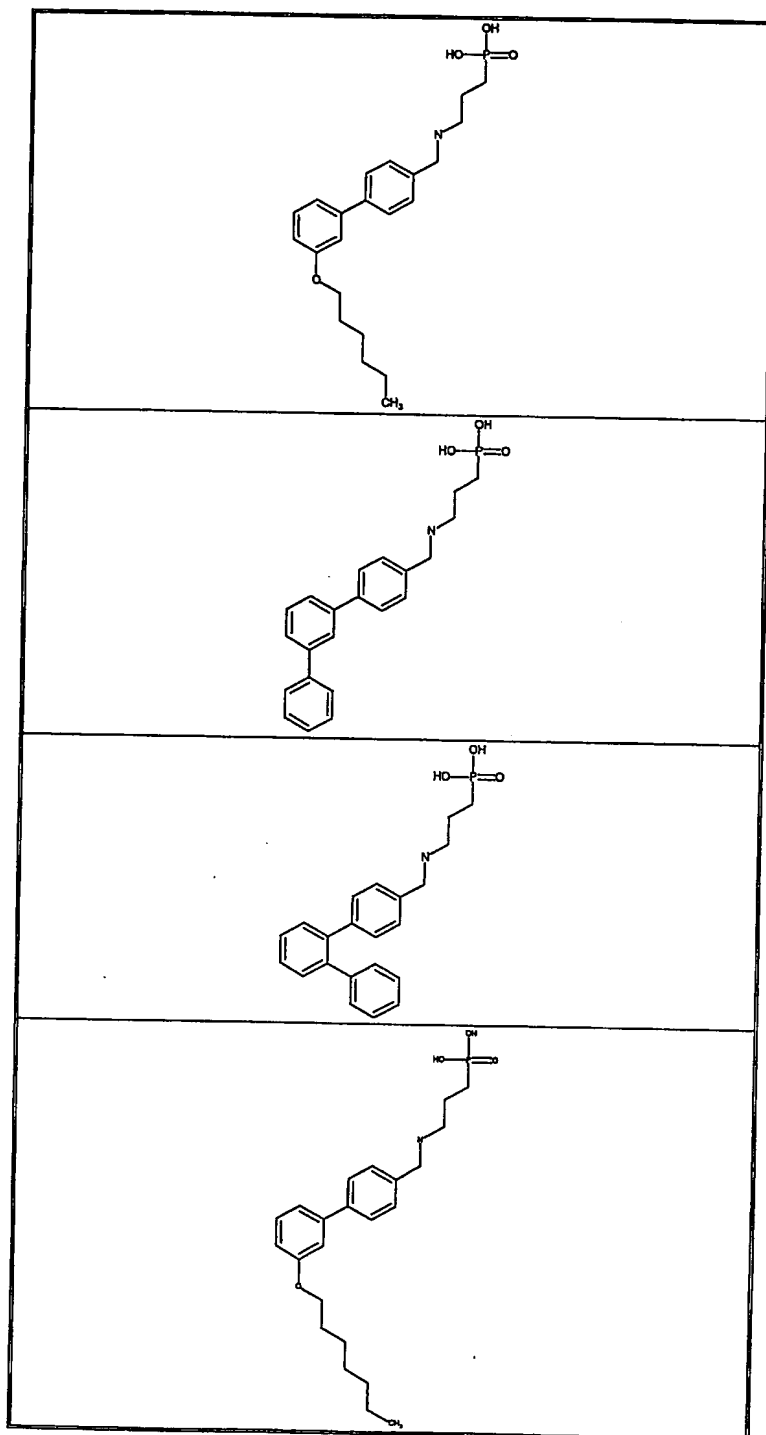


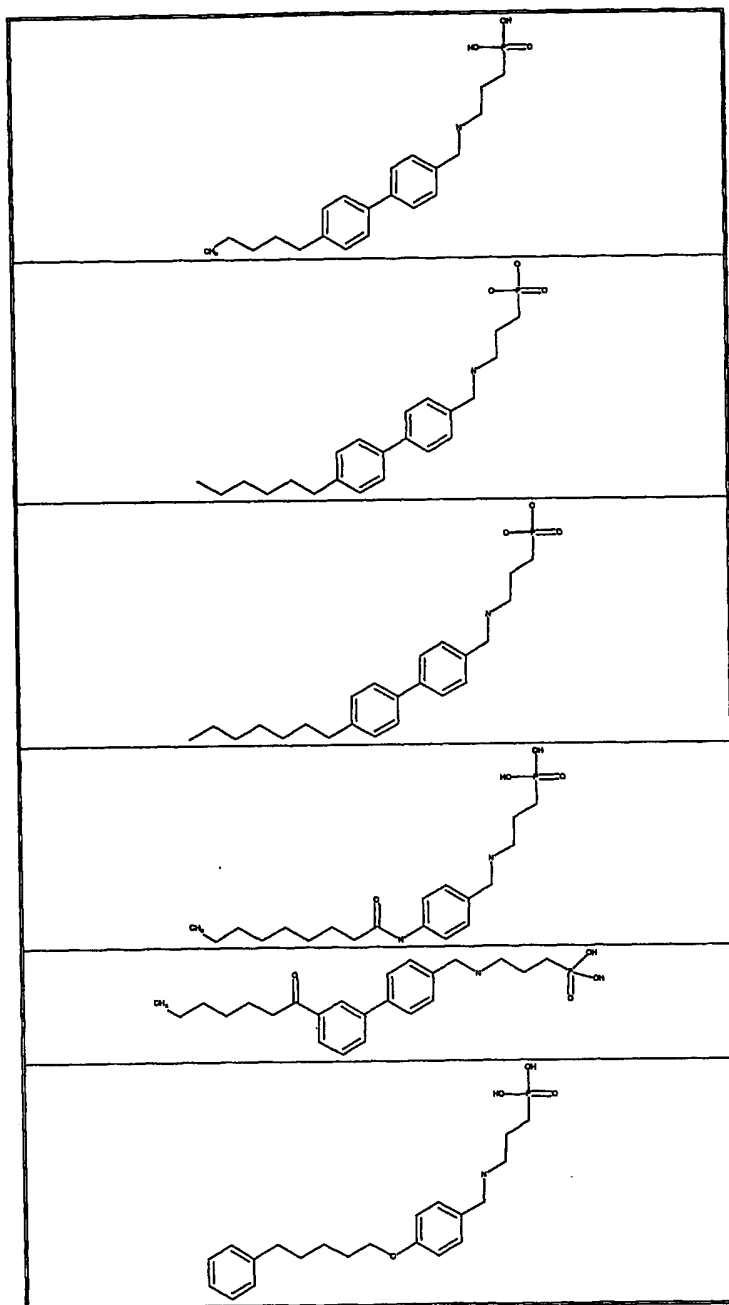


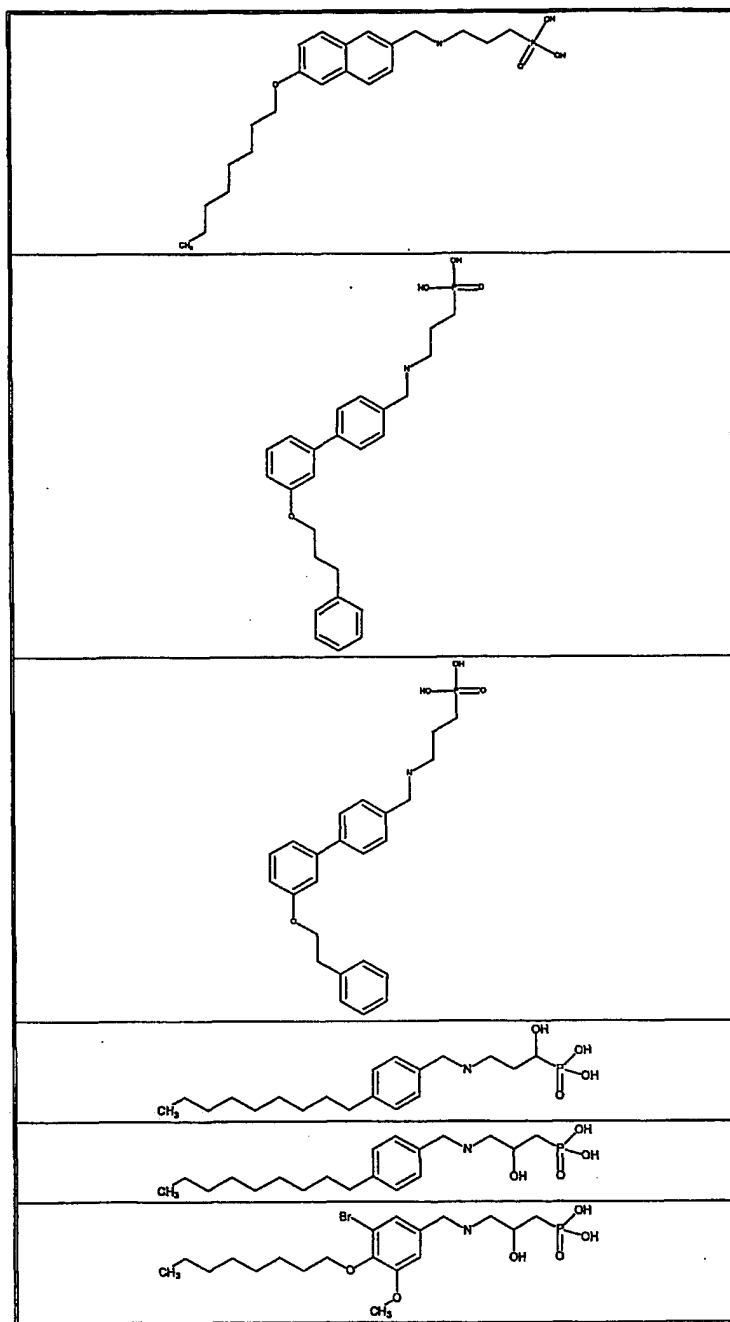


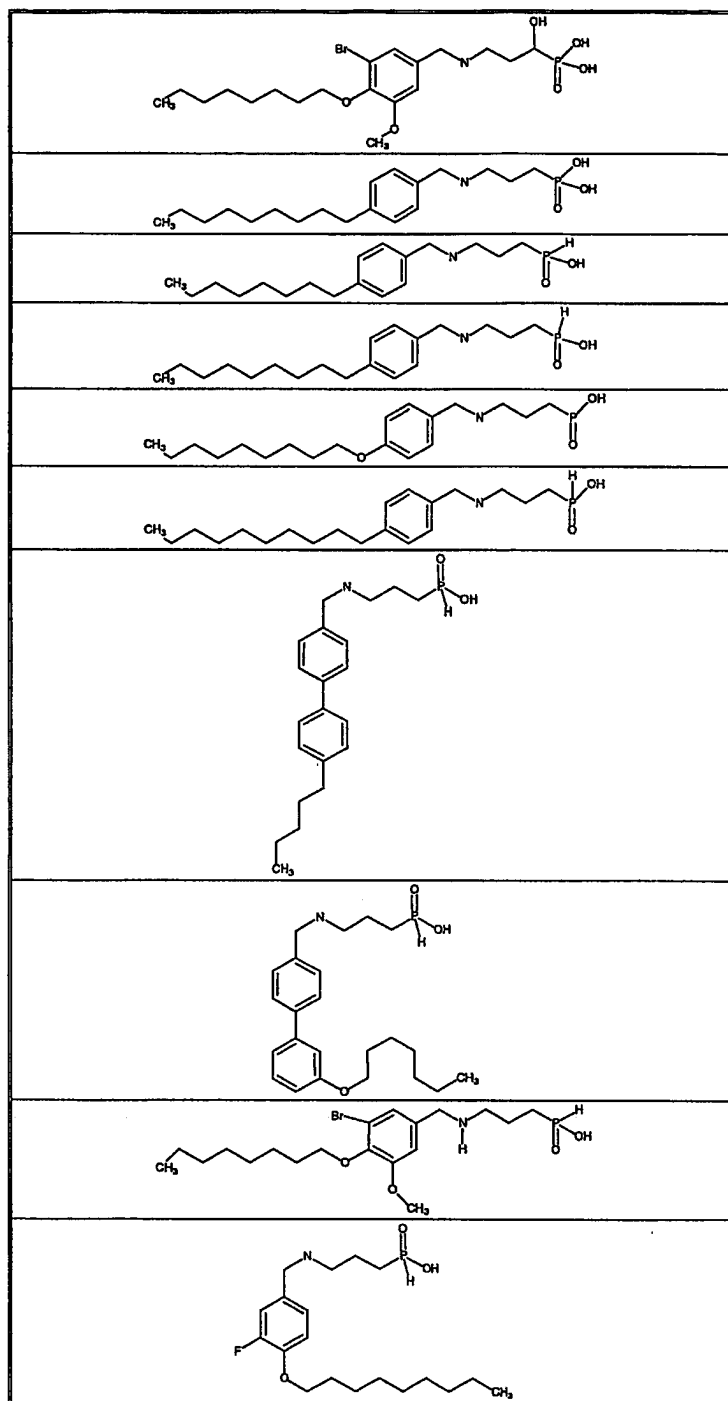


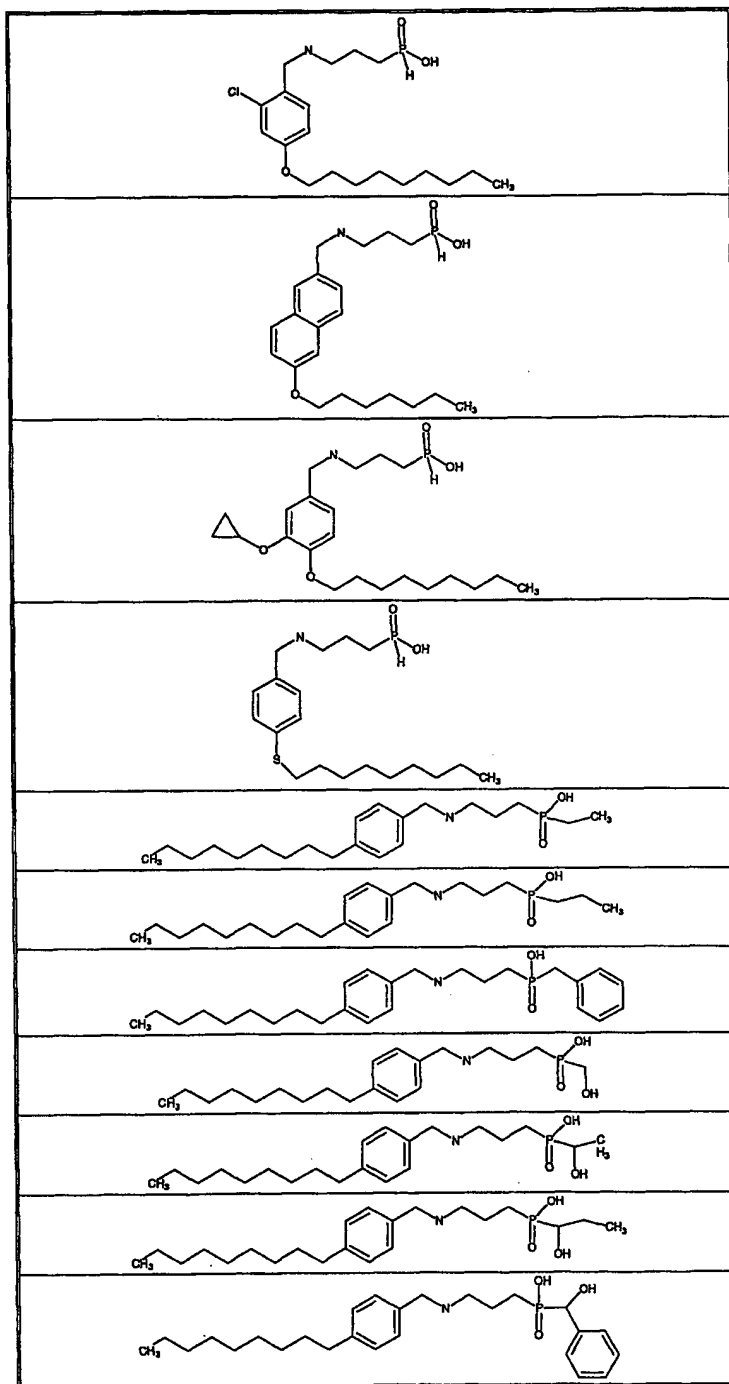


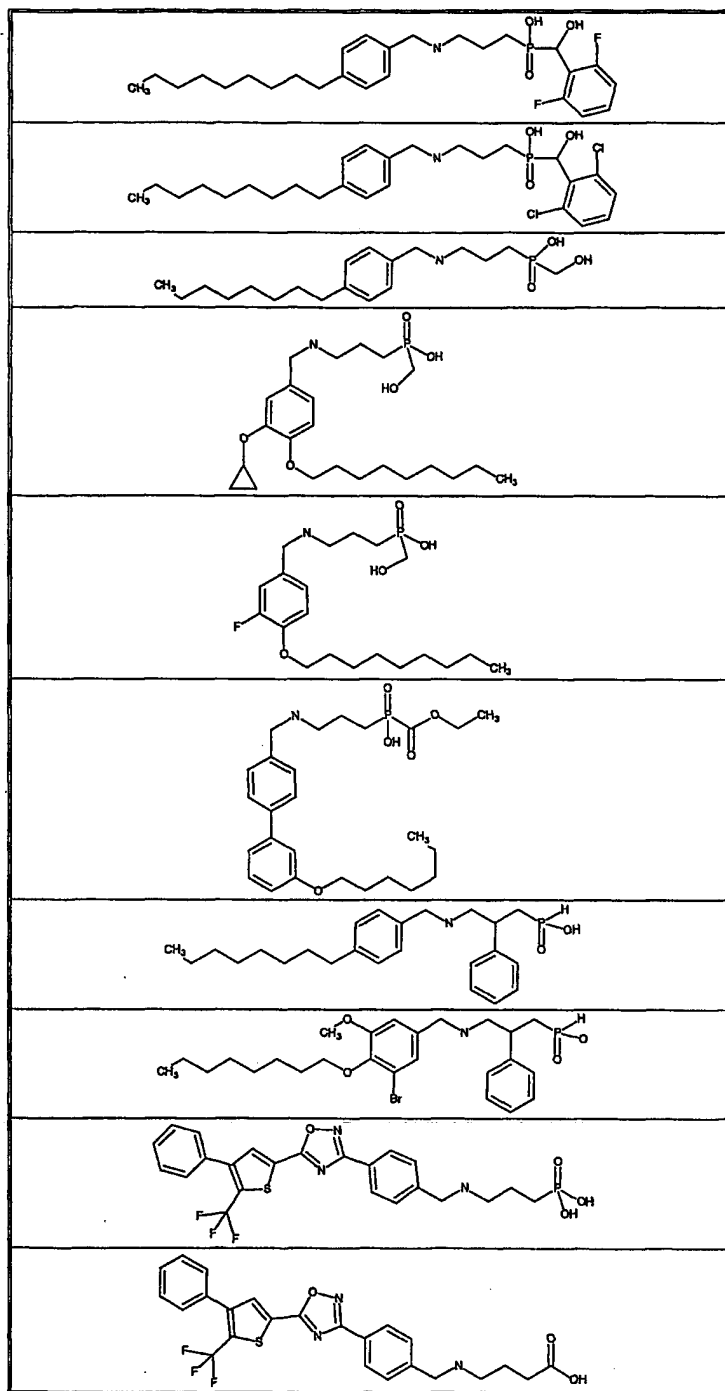


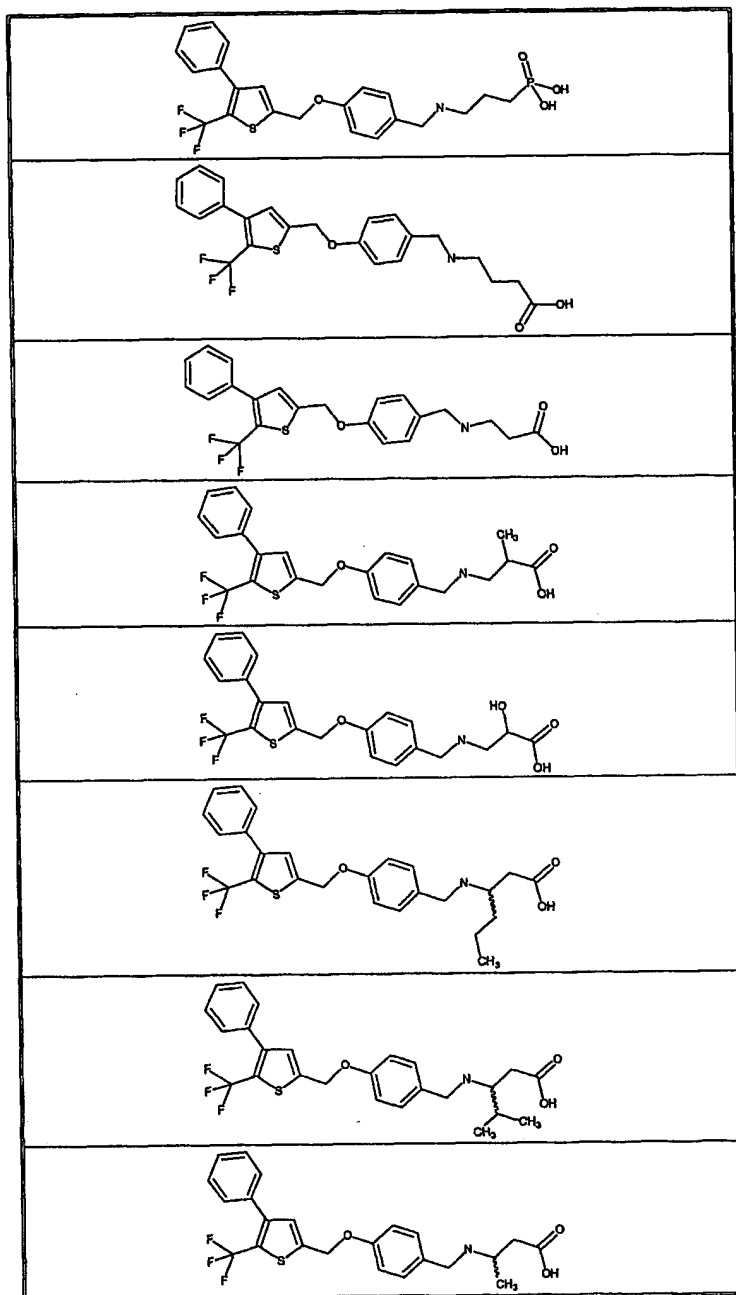


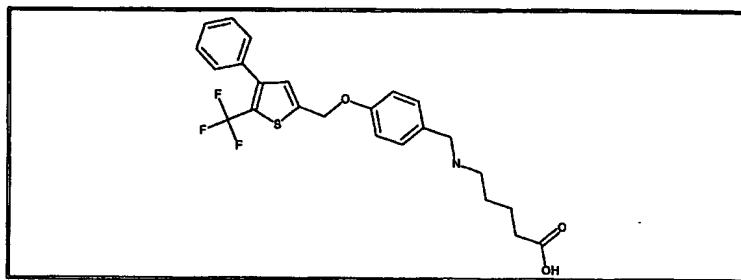












22. A method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound in accordance with Claim 1 in an amount that is effective for treating
5 said immunoregulatory abnormality.

23. The method according to Claim 22 wherein the immunoregulatory abnormality is an autoimmune or chronic inflammatory disease selected from the group consisting of: systemic lupus erythematosus, chronic
10 rheumatoid arthritis, type I diabetes mellitus, inflammatory bowel disease, biliary cirrhosis, uveitis, multiple sclerosis, Crohn's disease, ulcerative colitis, bullous pemphigoid, sarcoidosis, psoriasis, autoimmune myositis, Wegener's granulomatosis, ichthyosis, Graves ophthalmopathy and asthma.

15 24. The method according to Claim 22 wherein the immunoregulatory abnormality is bone marrow or organ transplant rejection or graft-versus-host disease.

25 25. The method according to Claim 22 wherein the immunoregulatory abnormality is selected from the group consisting of: transplantation of organs or tissue, graft-versus-host diseases brought about by transplantation, autoimmune syndromes including rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes, uveitis, posterior uveitis, allergic encephalomyelitis, glomerulonephritis,
20 post-infectious autoimmune diseases including rheumatic fever and post-infectious glomerulonephritis, inflammatory and hyperproliferative skin diseases, psoriasis, atopic dermatitis, contact dermatitis, eczematous dermatitis, seborrhoeic dermatitis, lichen planus, pemphigus, bullous pemphigoid, epidermolysis bullosa, urticaria,

- angioedemas, vasculitis, erythema, cutaneous eosinophilia, lupus erythematosus, acne, alopecia areata, keratoconjunctivitis, vernal conjunctivitis, uveitis associated with Behcet's disease, keratitis, herpetic keratitis, conical cornea, dystrophia epithelialis corneae, corneal leukoma, ocular pemphigus, Mooren's ulcer, scleritis, Graves' ophthalmopathy, Vogt-Koyanagi-Harada syndrome, sarcoidosis, pollen allergies, reversible obstructive airway disease, bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, dust asthma, chronic or inveterate asthma, late asthma and airway hyper-responsiveness, bronchitis, gastric ulcers, vascular damage caused by ischemic diseases and thrombosis, ischemic bowel diseases, inflammatory bowel diseases, necrotizing enterocolitis, intestinal lesions associated with thermal burns, coeliac diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, Crohn's disease, ulcerative colitis, migraine, rhinitis, eczema, interstitial nephritis, Goodpasture's syndrome, hemolytic-uremic syndrome, diabetic nephropathy, multiple myositis, Guillain-Barre syndrome, Meniere's disease, polyneuritis, multiple neuritis, mononeuritis, radiculopathy, hyperthyroidism, Basedow's disease, pure red cell aplasia, aplastic anemia, hypoplastic anemia, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, agranulocytosis, pernicious anemia, megaloblastic anemia, anerythroplasia, osteoporosis, sarcoidosis, fibroid lung, idiopathic interstitial pneumonia, dermatomyositis, leukoderma vulgaris, ichthyosis vulgaris, photoallergic sensitivity, cutaneous T cell lymphoma, arteriosclerosis, atherosclerosis, aortitis syndrome, polyarteritis nodosa, myocarditis, scleroderma, Wegener's granuloma, Sjogren's syndrome, adiposis, eosinophilic fascitis, lesions of gingiva, periodontium, alveolar bone, substantia ossea dentis, glomerulonephritis, male pattern alopecia or alopecia senilis by preventing epilation or providing hair germination and/or promoting hair generation and hair growth, muscular dystrophy, pyoderma and Sezary's syndrome, Addison's disease, ischemia-reperfusion injury of organs which occurs upon preservation, transplantation or ischemic disease, endotoxin-shock, pseudomembranous colitis, colitis caused by drug or radiation, ischemic acute renal insufficiency, chronic renal insufficiency, toxinsosis caused by lung-oxygen or drugs, lung cancer, pulmonary emphysema, cataracta, siderosis, retinitis pigmentosa, senile macular degeneration, vitreal scarring, corneal alkali burn, dermatitis erythema multiforme, linear IgA ballous dermatitis and cement dermatitis, gingivitis, periodontitis, sepsis, pancreatitis, diseases caused by environmental pollution, aging, carcinogenesis, metastasis of carcinoma and hypobaropathy, disease caused by histamine or leukotriene-C4 release, Behcet's disease, autoimmune hepatitis, primary

biliary cirrhosis, sclerosing cholangitis, partial liver resection, acute liver necrosis, necrosis caused by toxin, viral hepatitis, shock, or anoxia, B-virus hepatitis, non-A/non-B hepatitis, cirrhosis, alcoholic cirrhosis, hepatic failure, fulminant hepatic failure, late-onset hepatic failure, "acute-on-chronic" liver failure, augmentation of
5 chemotherapy effect, cytomegalovirus infection, HCMV infection, AIDS, cancer, senile dementia, trauma, and chronic bacterial infection.

26. The method according to Claim 22 wherein the
immunoregulatory abnormality is multiple sclerosis
10

27. The method according to Claim 22 wherein the
immunoregulatory abnormality is rheumatoid arthritis

28. The method according to Claim 22 wherein the
15 immunoregulatory abnormality is systemic lupus erythematosus

29. The method according to Claim 22 wherein the
immunoregulatory abnormality is psoriasis

30. The method according to Claim 22 wherein the
20 immunoregulatory abnormality is rejection of transplanted organ or tissue

31. The method according to Claim 22 wherein the
immunoregulatory abnormality is inflammatory bowel disease.
25

32. The method according to Claim 22 wherein the
immunoregulatory abnormality is a malignancy of lymphoid origin.

33. The method according to Claim 22 wherein the
30 immunoregulatory abnormality is acute and chronic lymphocytic leukemias and lymphomas.

34. A method of suppressing the immune system in a mammalian
patient in need of immunosuppression comprising administering to said patient an
35 immunosuppressing effective amount of a compound of Claim 1.

35. A pharmaceutical composition comprised of a compound in accordance with Claim 1 in combination with a pharmaceutically acceptable carrier.